transgenic progeny expressing any exogenous protein in oviduct and/or eggs in any and all offspring.

The Examiner's Action also states that the art at the time of filing the instant application is highly unpredictable because of the complexities of egg formation make the earliest stages of chick-embryo development relatively inaccessible and points out that ex-vivo transfection of blastodemal cells and reimplantation into an egg has not been show to transmit the transgene through germ-lines. The Examiner indicates that development of chicken embryonic stem cells that can be grown for longer periods in culture to allow targeted recombination events is highly unpredictable and that it is also unclear how a particular transgene would effect the development of mature birds in the production of transgenic eggs.

The Examiner's Office Action also notes that, although replication defective retroviral vectors have been used to obtain germ-line transmission of transgenes in a wide variety of tissues, tissue-specific expression has not been achieved. The Action further states that the Specification fails to show expression of any exogenous protein in the tubular gland cells of the oviduct or magnum tissue of any and all birds.

Applicants have amended independent claims 19, 27, 35, 44, and 53 – 55 to limit the claims to a particular bird, a chicken, in response to the concerns raised in the Office Action. Applicants respectfully point out, however, that the Specification teaches the production of exogenous protein in tubular gland cells of the oviduct because it is in those cells that the synthesis of egg white proteins are produced and deposited in the egg white (see Attachment A, Deeley et al, "Synthesis and Deposition of Egg Proteins in Manipulation of the Avian Genome," p. 205). Because the claims, as amended, do not limit the production of exogenous protein to only the tubular gland cells, but merely reflect protein is produced in these cells for secretion into the egg white, as taught by the Specification, the claims are not limited to tissue-specific protein expression.

Applicants have further amended independent claims 19, 27, 35, 44 and 53 to indicate that the exogenous proteins produced by the method of the present invention are Interferon,

Erythropoietin and GM-CSF and to specify the present invention uses an ALV retroviral vector driven by a constitutive promoter to produce the exogenous protein.

Applicants respectfully point out, however, that the present Specification, as confirmed by the declaration of Dr. Jeffrey Rapp submitted previously to the Examiner, teach the production of fully transgenic chickens (i.e., G2 offspring) by breeding chimeric founders. Applicants have provided data showing that the G1 and G2 progeny produce Interferon, Erythropoietin and GM-CSF in their serum, as well as in the egg white of eggs laid by transgenic hens. Further, Applicants show that, for the above-mentioned proteins, there have been no detrimental effects to the hens resulting from the expression of exogenous DNA in their genome.

By following the teachings in the present Specification, Applicants have successfully expressed the above-mentioned proteins, both in the serum of transgenic birds and in the egg white of eggs obtained from the transgenic hens. Accordingly, Applicants respectfully submit that independent claims 19, 27, 35, 54 –55, and 57 – 59, as amended, satisfy the requirements under 35 U.S.C. § 112, first paragraph, and respectfully request allowance.

The Examiner's Office Action rejects claims 25, 41 and 56 as being anticipated by Bosselman et al; under 35 U.S.C. 102 (b). Claim 56 is also rejected under 35 U.S.C. 103 (a) as being unpatentable over Bosselman et al, as applied to claim 25 and 41 above, and further in view of Sekellick et al.

Applicants have canceled claims 25, 41 and 56 and, therefore, respectfully submit that the remaining claims are patentable under 35 U.S.C. 102 (b) and 35 U.S.C. 103 (a).

In summary, Applicants submit that the claims presently in the application, as amended, are patentably distinct over the prior art of record and are in compliance with the enablement requirement under 35 U.S.C. § 112, first paragraph. Thus, it is submitted that the present Application is in condition for allowance, and favorable action is therefore respectfully requested.

The Examiner is invited to telephone the undersigned at his convenience, should only minor issues remain after consideration of the present amendment, to permit early resolution of same.

Attachments

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Applicant requests amendment of the claims in order to place the application in condition for allowance as follows:

Please amend claim 19 as follows:

19. (Amended) A transgenic [bird] chicken having a transgene in the genetic material of its germ-line tissue, wherein the transgene comprises an exogenous gene, selected from the group consisting of *interferon, erythropoietin* and *GM-CSF*, and a constitutive promoter, in operational and positional relationship to express said exogenous gene, and said exogenous gene is expressed in the tubular gland cells of the [avian] oviduct of the transgenic [bird] chicken.

Please amend claim 27 as follows:

27. (Twice Amended) A method for producing an exogenous protein in [an avian] a chicken oviduct, said protein selected from the group consisting of Interferon, Erythropoietin and GM-CSF, comprising:

providing a ALV retroviral vector that comprises a coding sequence and a constitutive promoter operably linked to said coding sequence, where[in] said promoter can effect expression of the coding sequence in the tubular gland cells of [an avian] a chicken oviduct;

creating transgenic cells by introducing said vector into [avian] chicken stage X embryonic [blastodermal] cells, wherein the vector sequence is inserted into the [avian] chicken genome; and

deriving a mature transgenic [avian] chicken from said transgenic cells, wherein tubular gland cells of the transgenic [avian] chicken express said coding sequence, resulting in the production of said exogenous protein.

Please amend claim 35 as follows:

35. (Thrice Amended) A method for producing [an avian] a chicken egg which contains exogenous protein, selected from the group consisting of Interferon, Erythropoietin and GM-CSF,comprising:

providing a ALV retroviral vector that comprises a coding sequence and a constitutive promoter operably linked to said coding sequence, wherein said promoter can effect expression of the coding sequence in the tubular gland cells of [an avian] a chicken oviduct;

creating transgenic cells by introducing said vector into [avian] chicken stage X embryonic blastodermal cells, wherein the vector sequence is inserted into the [avian] chicken genome; and

deriving a mature transgenic [avian] chicken from said transgenic cells, wherein the tubular gland cells of the transgenic [avian] chicken express the coding sequence, and the resulting protein is secreted into the oviduct lumen, so that the protein is deposited in the white of an egg.

Please amend claim 43 as follows:

43. (Amended) The transgenic [bird] chicken of Claim [42] 35, wherein said constitutive promoter is a cytomegalovirus promoter.

Please amend claim 44 as follows:

44. (Amended) A transgenic [bird] chicken having a transgene in the genetic material of the tubular gland cells of its magnum, wherein the transgene comprises an exogenous gene and a promoter, in operational and positional relationship to express said exogenous gene, whereas said exogenous gene is selected from the group consisting of Interferon, Erythropoietin and GM-CSF, and said exogenous gene is expressed in the tubular gland cells of the transgenic [bird] chicken.

Please amend claim 45 as follows:

45. (Amended) The method of claim [29] 27, wherein said constitutive promoter is the cytomegalovirus promoter.

Please amend claim 53 as follows:

53. (Twice Amended) A transgenic [bird] chicken having a transgene in the genetic material of its germ-line tissue, wherein the transgene comprises an exogenous gene, selected from the group

consisting of Interferon, Erythropoietin and GM-CSF, and a constitutive promoter, in operational and positional relationship to express said exogenous gene, [wherein] and said exogenous gene is expressed in the tubular gland cells of the chicken oviduct of the transgenic [bird] chicken, and wherein the protein encoded by said exogenous gene is deposited in eggs of said transgenic [bird] chicken.

Please amend claim 54 as follows:

54. (Twice Amended) A transgenic [bird] chicken having a transgene in the genetic material of the tubular gland cells of its magnum, wherein the transgene comprises an exogenous gene, selected from the group consisting of Interferon, Erythropoietin and GM-CSF, and a constitutive promoter, in operational and positional relationship to express said exogenous gene, wherein said exogenous gene is expressed in the tubular gland cells of the transgenic [bird] chicken, and where[in] the protein encoded by said exogenous gene is deposited in eggs of said transgenic [bird] chicken.

Please amend claim 55 as follows:

55. (Twice Amended) A method for producing protein, comprising:

providing a ALV retroviral vector that comprises a coding sequence, selected from the group consisting of Interferon, Erythropoietin and GM-CSF, and a constitutive promoter operably linked to said coding sequence, wherein said promoter can effect expression of the coding sequence in the tubular gland cells of an [avian] chicken oviduct;

creating transgenic cells by introducing said vector into chicken stage X [avian] embryonic blastodermal cells, wherein the vector sequence is inserted into the [avian] chicken genome;

deriving a mature transgenic [avian] chicken from said transgenic cells, wherein the tubular gland cells of the transgenic [avian] chicken express the coding sequence, and the resulting protein is secreted into the oviduct lumen, so that the protein is deposited in the white of an egg; and

[i]Isolating said protein from said egg.

Please amend claim 57 as follows:

57. (Amended) [An] [I]Interferon isolated from an egg produced by a method of claim 35.